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Case Report

Gingival enlargement as oral manifestation in acute myeloid leukemia patient

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ABSTRACT

Background: *Acute myeloid leukemia (AML) is a bone marrow cancer, a malignant disease that triggering the cells develops into different types of blood cells. It is widely recognized that the main manifestation of AML could be gingival hyperplasia and bleeding. Occasionally, an initial diagnosis of leukemia is made after a dental examination. In relation to systemic diseases, gingival enlargement could constitute the intensification of an existing inflammation initiated by dental plaque, or a manifestation of the systemic disease independent of the inflammatory condition of the gingiva. Gingival enlargement negatively affects the quality of life, especially nutritional intake.* ***Purpose:*** *This study aimed to report on gingival enlargement in AML patients, dental management of this condition and considerations when treating patients.* ***Case:*** *A 46 year-old woman diagnosed with AML who chiefly complained of gingival enlargement in all parts of the mouth which restricted her nutritional intake.* ***Case management:*** *The subject attended the clinic twice where nonsurgical treatment for the gingival enlargement, supragingival scaling and dental health education to maintain her oral hygiene was carried out. Unfortunately, she did not return for follow-up appointments due to having already passed away. Information about AML and its relation to gingival enlargement contained in the literature is also reviewed.* ***Conclusion:*** *In conclusion, gingival enlargement represents one oral manifestation of AML. This condition is related to and affects the nutritional intake of the patient.*

Keywords: *acute myeloid leukemia; gingival enlargement; blast cells; periodontal systemic disease related*

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INTRODUCTION

Acute myeloid leukemia (AML) is a bone marrow cancer, a malignant disease that triggering the cells develops into different types of blood cells. Generally, AML disease afflicts older person and is remarkably in individuals below the age of 45. The average age of a patient with AML is approximately 67 years. AML is commonest in men than women, but the average lifetime risk for both sexes is less than half of 1%. The site of AML disease is bone marrow where new blood cells are produced and it usually circulates quickly into the blood. Consequently, it can sometimes spread to other parts of the body, including the central nervous system (brain and spinal cord), liver, lymph nodes, spleen, and testicles. In term of the acute leukemia, the immature blood cells of cancerous cells are called blasts. These normal blast cells divide quickly which cause the leukemias fast-growing. Leukemia cells do not stop dividing when normal blast cells would.[1,2] It presents with marrow failure and cytopenia. Symptoms include fever, fatigue, pallor, mucosal bleeding, petechiae, and local infections.[3]

AML presents oral manifestations which represent a number of the diagnostic indicators of the disease. The oral symptoms of acute leukemia include the swollen gingiva, petechiae, mucosal anemic, oral ulceration, spontaneous gingival bleeding candidacies and herpetic infections.[4] The first diagnosis of leukemia to be made after a dental examination might be because of the main oral appearance of AML are the bleeding and hyperplasia of gingiva.[5–7] From the surveillance, epidemiology, and end results (SEER) data in year 2011 for AML during were estimated to be 17.5 per 100,000 (n=7,245) among the š65-year-old population and 1.8 per 100,000 (n=4,864)

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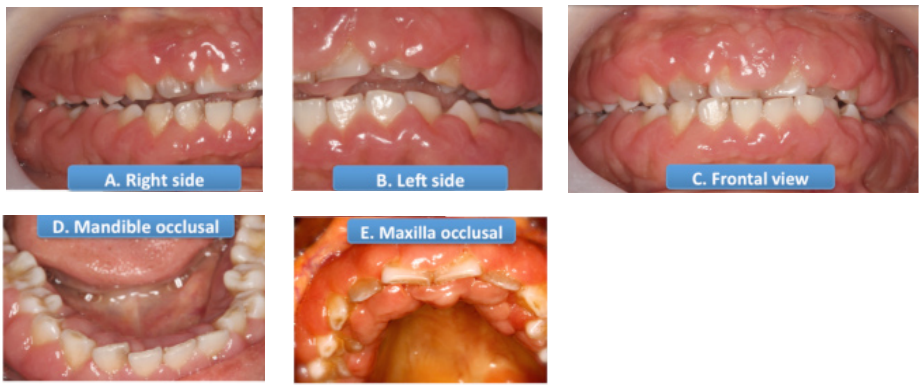

Figure 1. Clinical view of gingival enlargement in AML patient. (a) right side; (b) left side; (c) frontal view; (d) maxilla occlusal; (e) mandible occlusal. From a clinical viewpoint, The condition of almost all the tooth surface in premolar and molar region were covered by enlargement of the gingiva. The color was bluish red in the gingival margin.

for those <65 years old.[5] The term of gingival hyperplasia is commonest in acute, rather than chronic, leukemia. Whilst, it is unpredictable in any individual patient for progress of gingival infiltration.[8]

The enlargement of the gingiva could constitute the compounding of an existing inflammation initiated by dental plaque or a manifestation of a systemic disease which is independent of the inflammatory status of the gingiva.[9] Oral manifestations of leukemia may include bleeding, oral ulcerations, leukemic infiltration until periodontal infections. The expression of these symptoms is less in chronic than acute and subacute forms of leukemia.[9]

A dentist's role in identifying oral manifestation of AML is central. Firstly, a diagnosis of leukemia is occasionally established after a dental examination. The dentist's role is to identify leukemic disease by means of oral examination, and referral to an internist or oncology department. Second, a dentist plays an important role in patient education about the importance of maintaining oral health and advising about the oral manifestation that may affect the quality of life.[10]

The case of a female patient diagnosed with AML and complaining chiefly of generalized gingival enlargement which affected her nutritional intake was reported. The internist referred the patient for a dental consultation to locate the focus of infection and gum infiltration. The purpose of this report was to explain the cases of gingival enlargement in AML patients, dental management of this condition and considerations connected with treating the patient.

CASE

A 46 year-old-female attended the Periodontics Specialist Clinic, Faculty of Dentistry, Universitas Indonesia, following referral by an internist at Cipto Mangunkusumo Hospital in order to locate the focus of infection and gum infiltration. The individual concerned was diagnosed with AML, her chief complaint being bleeding gums during the previous month. She presented symptoms including: an enlarged gum, difficulty in swallowing and constant pain. According to her medical history, prior to the previous three months, when she had suffered from fever, mild weight loss and loss of appetite the patient had appeared normal.

In the objective examination, the patient was in a good general condition, good communication, and had signs of anemia with the skin look pale. On extraoral examination, there was no abnormality. On intraoral examination, generalized gingival enlargement was noticed in upper and lower arches, buccally and lingually or palatally, and reached half of teeth surface. The color was pink, with plaque and supra and subgingival calculus (Figure 1).

CASE MANAGEMENT

On the patient's first consultant of October 2nd 2015, an initial therapy for periodontal treatment including dental health education, supra-gingival scaling, and antimicrobial therapy using chlorhexidine 0.12% to improve oral hygiene was conducted. The patient was referred to an oral medicine specialist for an oral lesion examination and sent back to the internist to potentially undergo a gingivectomy. Based on the findings of the systemic and intraoral examinations, the patient was advised of the desirability of a routine blood test.

On October 22nd, 2015, the results of a blood check and flow cytometry were reported by the Department of Pathology Clinic (Table 1). The contents of the table show that the highest percentage of leucocyte types was that of blast cells (73%). The result of the flow cytometry confirmed the presence of a positive marker in CD 33, CD 34, CD 117, HLA-DR, CD 13 (Figure 2). The interpretation from the Department of Pathology was myeloid lineage.

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Table 1. The result of hematologic findings in molecular diagnostic of leucocytes

Type of Leucocytes	Result	Normal value	Unit
Basophil	0.0	0 – 1	%
Eosinophil	0.0		%
Neutrophil rod	0.0	2 – 6	%
Neutrophil segment	1.5	50 – 70	%
Limphocyte	7.0	20 – 40	%
Monocyte	2.5	2 – 8	%
Blast	73.0		%
Pro mielocyte	0.0		%
Pro limphocyte	0.0		%
Pro monocyte	0.0		%
Mielocyte	0.0		%
Metamielocyte	0.0		%
Rubriblast	0.0		%
Prorubricyte	1.0		%
Rubricyte	4.0		%
Metarubricyte	3.0		%
Plasmocyte	7.5		%
Histiocyte	0.5		%

The patient was subsequently scheduled for chemotherapy treatment.

On December 9th, 2015, the patient presented the symptom of almost all premolar and molar region tooth surfaces being covered by an enlargement of the gingiva. The color was bluish red in the gingival margin. The patient was recommended to maintain oral hygiene and a consultation letter was sent to her internist doctor enquiring about the possibility of conducting a gingivectomy if pre-chemotherapy hematologic values reached the minimum required levels. However, unfortunately, the patient had already passed away.

DISCUSSION

AML in other term used as acute myelogenous leukemia, acute myeloblastic leukemia, acute granulocytic leukemia or acute nonlymphocytic leukemia, is a bone marrow fast-growing cancer. The fast growing means AML occurs when bone marrow produces blasts, cells that have not yet wholly matured, which normally develop into white blood cells. Unfortunately, these cells do not grow and are unable to ward off infection. Chemotherapy, radiation therapy, stem cell transplant and immunotherapy are treatment choices of AML.[1–3] In 1997, based on WHO classification, AML was sub-divided into four groups which are AML with recurrent cytogenetic translocations, AML with myelodysplasia-related features, therapy-related AML and myelodysplastic syndromes and non-specific AML.[12] Several forms of treatment may be applied for people suffering from the condition. Chemotherapy is the primary treatment for AML, occasionally in tandem with a targeted therapy drug. Other drugs may also be used to treat people with acute promyelocytic leukemia (APL). In extraordinary condition, surgery and radiation therapy may be resorted.[1]

Gingival enlargement in AML patients is one case that a dentist should understand and treat with appropriate remedial measures. Swelling of the gingiva is a standard clinical feature of the condition. The term "gingival enlargement" merely describes the clinical finding, rather than also seeking to offer an explanation of its fundamental nature.[3]

The clinical findings made from periodontal examination in patient majority lead to diagnosis of AML as oral manifestations of the disease.[12] In some instances, AML could first be identified by a dentist or periodontist, following a chief complaint of gingival enlargement.[13] Without the sharing of knowledge of the patient's condition, the dentist will apply treatment potentially aggravating it, thereby possibly exacerbating acute symptoms. In the most extensive review of the topic, observation of gingival enlargement in AML patient range in the frequency of 3% to 5% among 1,076 patients receiving anti-leukemia chemotherapy at a referral center.[8]

Oral manifestations of leukemia may include, bleeding, oral ulcerations, leukemic infiltration until periodontal infections. Infiltration of leukemic cells into the gingiva and, but less frequently to the alveolar bone. The

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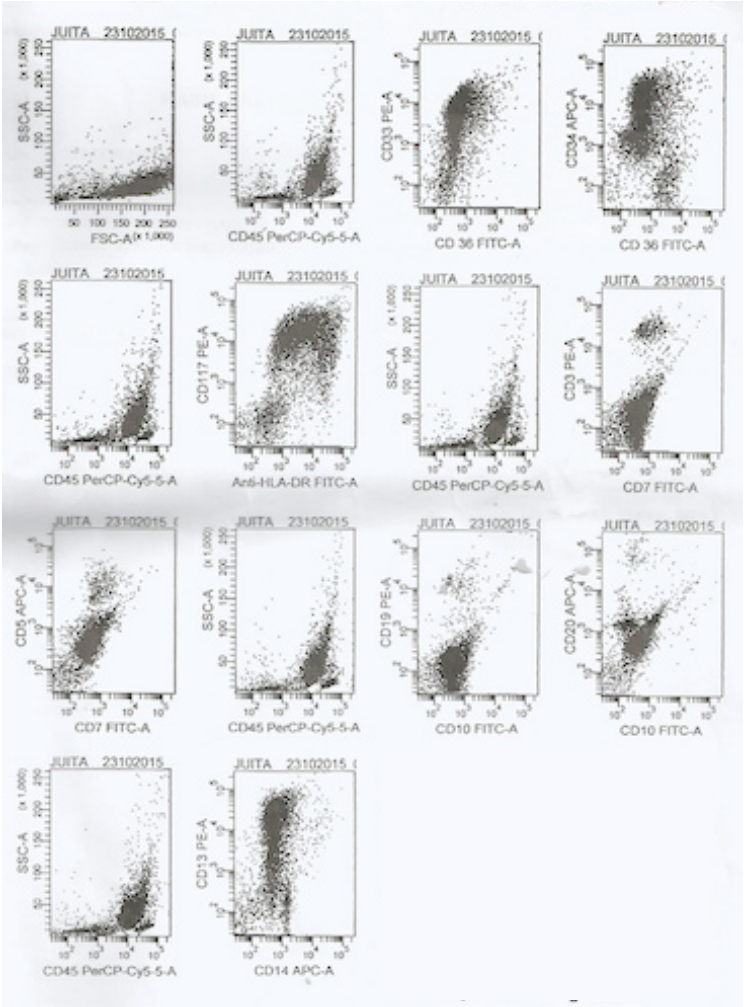

Figure 2. The results of flow cytometry show the positivity of CD 33, CD 34, CD 117, HLA DR and CD 13 which represent the myeloid lineage cell.

accumulation of immature blast cells in the gingiva is related to tooth surface with bacterial plaque. Leukemic gingival enlargement consists of a primary infiltration of the gingival corium by leukemic cells, this increases the gingival thickness resulting gingival pockets in which bacterial plaque accumulates. This condition initiating a secondary inflammatory lesion that role to the enlargement of the gingiva.[9]

The observation result of AML-M4 and M5 subtypes patients that are the leukemic cells are monocytic. Monocytes has strong chemo attractant ability to infiltrate tissues.[6] In this study, the case was mild periodontitis, but low-level antigens derived from periodontal bacteria acted as chemo attractants for myelomonocytic leukemic cells. In fact, the observation of notable mucosal enlargement only appears in the gingiva. The gingival enlargement manifested from leukemia may involve the accumulation of blast cells in the gingiva by chemo attractants derived from periodontal pathogens. Gingival enlargement as a rule be more severe in patients with severe periodontitis, which is often observed in AML-M4 and M5.[6]

Under microscopic examination, the gingiva was observed to be predominantly infiltrated by immature leucocytes in the marginal gingiva, and also attached gingiva. Indication of ectopic hematopoiesis could be seen as mitotic figures. The leukemic cells supplant normal connective tissue components of the gingiva. The feature of the cells depends on the type of leukemia. The cellular accumulation is denser in all layers of reticular connective tissue. The epithelium presents various changes and may be thinned or hyperplastic.[9]

The planning of periodontal treatment in AML patients should consider the hematologic values of the patient. The role of the dentist should be conducted at three different stages: pre-antineoplastic treatment, during antineoplastic treatment, and post-antineoplastic treatment.[14] In this case, the patient was undergoing pre-antineoplastic treatment that necessitates proper nutritional intake to promote an excellent health condition.

In the pre-antineoplastic treatment of AML, dental

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Table 2. Minimum haematological values for performance of invasive procedures in pre-chemotherapy treatment patients according to the US National Cancer Institute, 20115

Platelet counts	Neutrophil counts
>60,000 cell/mm^3: without additional support.	>2,000 cell/mm^3: without the need for antibiotic prophylaxis.
30,000 to 60,000 cell/mm^3 : optional transfusion for non-invasive procedure.	1,000 to 2,000 cell/mm^3: antibiotic prophylaxis (low risk).
<30,000 cell/mm^3: Platelets should be transfused 1 h before the procedure. Obtain immediate post-infusion platelet count; transfuse regularly to maintain counts >30,000–40,000 cell/mm^3 until healing begins.	<1,000 cell/mm^3: antibiotic prophylaxis with Amikacin 150 mg/m^2 1 h before surgery and Ticarcillin 75 mg/Kg IV 1 h before surgery. Repeat both 6 h post-operative.

treatment is based on priorities and should be directed towards meeting acute needs. The identifiable aims of dental treatment include: preventing potential infection from an oral condition, education for maintaining oral health and raising awareness about the possibility of specific issues relating to oral tissue such as gingival enlargement.[10] Shankarapillai et al. reported their research into the periodontal health parameters in young adults with AML in Kerala, South India. The research confirmed around three-quarters of the patients to be suffering from either reasonable or poor oral hygiene. The association between dental plaque levels and both gingival overgrowth and periodontal index was observed resulted statistically significant ($p<0.001$). The resulting conclusion was that poor oral hygiene is a risk factor for leukemic gingival overgrowth and defect in periodontal disease.[15] In the case of the patient reported here, the improvement of oral hygiene proved critical to periodontal healing.

A decision to undertake invasive procedure gingivectomy will be considered if the minimum hematologic values have reached the required level. With regard to the risk of bleeding and severe infection associated with invasive procedures in the oral cavity, there are certain protocols that emphasize the importance of evaluating individual hematological indices, mainly: neutrophils and platelets. The US National Cancer Institute argues that interventions at this stage should be directed at the treatment of lesions in the oral mucosa, the lesions of carious and endodontic, periodontal disease, unfitting dentures, orthodontic appliances, temporomandibular joint disorder and dysfunction of the saliva.[16] The minimum hematologic values in pre-chemotherapy treatment patients of the US National Cancer Institute featured in Table 2, show minimum platelet counts >30,000 cells/mm3 and minimum neutrophil counts <1,000 cells/mm3. According to Haytac *et al*. a neutrophil count of 1,500 cells/mm3 and platelets of 40,000 cells/mm3 are required in order for periodontal probing or extractions to be performed. The procedures must be carried out under antibiotic cover and at least three days before the start of chemotherapy (approximately ten days before the granulocyte count falls below 500 cells/mm3). In cases when this is not possible, dental treatment should be postponed until the hematological indices increase.[17]

A dentist or periodontist could play the most significant role in the systemic condition of the patient as, potentially, the first medical staff who diagnoses leukemia. As soon as the potential conditions are detected, the patients should be referred to a hematologist-oncologist for early treatment to cure the leukemia. A dentist should be involved at three different stages of the dental management of the patient which are pre-antineoplastic treatment, ongoing anti-neoplastic treatment and post-treatment care. The primary goal of dental treatment of an AML patient is oral hygiene maintenance. Invasive procedures, including periodontal probing, should be completed if minimum hematologic values are required. In conclusion, gingival enlargement represents one oral manifestation of AML. This condition is related to and affects the nutritional intake of the patient.

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